PB89-123400

Health and Environmental Effects Profile for 1,4-Naphthoquinone

(U.S.) Environmental Protection Agency
Cincinnati, OH

Sep 86

U.S. Department of Commerce
National Technical Information Service
NTIS

PB89-123400

EPA/600/X-86/257
September 1986

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR 1,4-NAPHTHOQUINONE

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL INFORMATION SERVICE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)		
1. REPORT NO. EPA/600/X-86/257	2.	3. RECIPIENT'S ACCESSION NO PB89 123400/AS
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for 1,4-Naphthoquinone		5. REPORT DATE September 1986 6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)		8. PERFORMING ORGANIZATION REPORT NO
9. PERFORMING ORGANIZATION NAME AND ADDRESS		10. PROGRAM ELEMENT NO. 11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268		13. TYPE OF REPORT AND PERIOD COVERED 14. SPONSORING AGENCY CODE EPA/600/22
15 SUPPLEMENTARY NOTES		

16 ABSTRACT

The Health and Environmental Effects Profile for 1,4-Naphthoquinone was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine a Reference Dose (RfD) or a carcinogenic potency factor for 1,4-naphthoquinone.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. Existing data are insufficient to determine an RQ value.

17. KEY WORDS AND DOCUMENT ANALYSIS		
a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 43
	20. SECURITY CLASS (This page) Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1985.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic exposures. An RfD is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, RfDs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

EXECUTIVE SUMMARY

1,4-Naphthoquinone is a solid at room temperature. No sites for production of this compound were reported in the United States; however, five importers were listed in the TSCA Inventory (U.S. EPA, 1977). In 1983, a total of 61,260 pounds of 1,4-naphthoquinone were imported (USITC, 1984). 1,4-Naphthoquinone is used as a polymerization regulator for rubber and polyester resins, in the synthesis of dyes and pharmaceuticals, and as a fungicide and algicide (Hawley, 1981).

In water, 1,4-naphthoquinone can undergo photoreduction by reaction with HO radicals (Hashimoto et al., 1975). Potential for photolysis is also suggested by absorption of light wavelengths in the environmentally significant range (Finley, 1982). U.S. EPA (1985) reported that elimination or degradation and volatilization of 1,4-naphthoquinone from water is not expected. BCFs estimated from physical properties suggest that there is a slight potential for bioaccumulation to occur in aquatic organisms. The estimated concentration in bottom sediment is 13.8 times greater than its concentration in ambient water (U.S. EPA, 1985).

In air, potential for photoysis is indicated by a UV absorption maximum (in acetonitrile) at a wavelength of 330 nm (Finley, 1982).

Sims and Overcash (1983) reported a significantly short biodegradation half-life for 1,4-naphthoquinone in soil; however, information was insufficient for adequate evaluation of this transformation mechanism. The compound has been predicted to be slightly to moderately mobile in soils, based on estimated K_{oc} values.

No information was found on the presence of 1,4-naphthoquinone in the environment. Potential sources of 1,4-naphthoquinone release are during transport, processing, use, degradation of certain naphthalene derivatives (i.e., carbaryl), production of phthalic anhydride by air-oxidation of naphthalene and particulate emissions during fluidized-bed coal combustion (U.S. EPA, n.d.; Paris et al., 1975; Rajagopal et al., 1984; Hunt et al., 1982).

There is very little information available concerning the toxicity of 1,4-naphthoquinone to aquatic organisms. Concentrations of 0.3-0.6 mg/ℓ were reported to be toxic to several fish species (Fitzgerald et al., 1952). The most sensitive aquatic species tested was the green alga, Dunaliella bioculata, with a 50- to 72-hour LC_{50} of 0.011 mg/ℓ (Heldal et al., 1984).

Pertinent data regarding the absorption, distribution or excretion of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

In vitro studies with rat liver microsomes and hepatocytes suggest that 1,4-naphthoquinone may be metabolized by one electron reduction to the naphthosemiquinone radical, which may covalently bind with cellular molecules or enter a redox cycle with molecular oxygen, thereby generating active oxygen species (Doherty and Cohen, 1984; Doherty et al., 1984; Thornalley et al., 1984). The presence of these metabolites may explain the cytotoxic and antitumorigenic properties of the compound.

Takizawa (1940a,b) suggested that dermal application of 0.25 or 0.1% 1,4-naphthoquinone in benzene to mice every 1 or 2 days for what appears to be 200 days produced low incidences of local papillomas and carcinomas. The significance of these results cannot be ascertained, however, because tumor incidences were not specifically reported and control data were incomplete in the available summary (Hartwell, 1963) of these studies.

1,4-Naphthoquinone was not mutagenic to S. typhimurium strains TA97, TA98 and/or TA100 when tested in plate incorporation assays with or without S-9 metabolic activation preparation (Sakai et al., 1985; Onodera et al., 1982).

Information regarding the teratogenicity of 1,4-naphthoquinone was not located. 1,4-Naphthoquinone did not interrupt pregnancy when administered to mice by gavage at doses up to 600 µg/day on days 6-12 of gestation (Wiesner et al., 1958) or affect the estrous cycle of rats when subcutaneously injected at doses of 10 mg/day for 14 days (Rosen and Millman, 1955).

Slyusar et al. (1962) reported that biweekly subcutaneous injections of 0.025 mg/kg for 2.5-5 months produced increased spleen, liver and adrenal weights, dystrophic histological changes in the liver and myocardium, decreased serum albumin and cholinesterase activities, methemoglobinemia, anemia, erythrocytopenia, decreased plasma -SH groups and decreased vitamin C content in unspecified organs. Additional information regarding the subchronic or chronic toxicity of 1,4-naphthoquinone was not located, although consistent hemolytic effects have been reported in in vitro studies with human erythrocytes (Miller and Smith, 1970, 1971). Single dose oral LD_{50}s in the range of 100-500 mg/kg have been reported for mice (Ansbacher et al., 1942; Schafer and Bowles, 1985).

Calculation of an RfD, RQ or carcinogenicty potency factors (q_1^* and F) is precluded by the lack of data and limitations in data quality and routes of exposure. Carcinogenicity data are inadequate; therefore, 1,4-naphthoquinone is classified in IARC Group 3 and CAG Group D (U.S. EPA, 1984).

TABLE OF CONTENTS

		Page
1.	INTRODUCTION	1
1.1.	STRUCTURE AND CAS NUMBER	1
1.2.	PHYSICAL AND CHEMICAL PROPERTIES	1
1.3.	PRODUCTION DATA	2
1.4.	USE DATA	2
1.5.	SUMMARY	2
2.	ENVIRONMENTAL FATE AND TRANSPORT PROCESSES	3
2.1.	WATER	3
2.1.1.	Hydrolysis	3
2.1.2.	Oxidation	3
2.1.3.	Photolysis	3
2.1.4.	Microbial Degradation	3
2.1.5.	Volatilization	3
2.1.6.	Bioaccumulation	4
2.1.7.	Adsorption	4
2.2.	AIR	4
2.3.	SOIL	4
2.3.1.	Chemical Degradation	4
2.3.2.	Microbial Degradation	4
2.3.3.	Volatilization	5
2.3.4.	Adsorption	5
2.4.	SUMMARY	5
3.	EXPOSURE	7
4.	PHARMACOKINETCS	8
5.	EFFECTS	9
5.1.	CARCINOGENICITY	9
5.2.	MUTAGENICITY	10
5.3.	TERATOGENICITY	10
5.4.	OTHER REPRODUCTIVE EFFECTS	10
5.5.	CHRONIC AND SUBCHRONIC TOXICITY	10
5.6.	OTHER RELEVANT INFORMATION	11
5.7.	SUMMARY	11

TABLE OF CONTENTS (cont.)

		Page
6.	AQUATIC TOXICITY	13
6.1.	ACUTE	13
6.2.	CHRONIC	13
6.3.	PLANTS	13
6.4.	RESIDUES	15
6.5.	OTHER RELEVANT INFORMATION	15
6.6.	SUMMARY	15
7.	EXISTING GUIDELINES AND STANDARDS	16
7.1.	HUMAN	16
7.2.	AQUATIC	16
8.	RISK ASSESSMENT	17
9.	REPORTABLE QUANTITIES	18
9.1.	REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY	18
9.2.	WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY	20
10.	REFERENCES	21
APPENDIX:	LITERATURE SEARCHED	28

LIST OF TABLES

No.	Title	Page
2-1	Estimated K_{OC} Values for 1,4-Naphthoquinone	6
6-1	Toxicity of 1,4-Naphthoquinone to Aquatic Plants.	14
9-1	1,4-Naphthoquinone: Minimum Effective Dose (MED) and Reportable Quantity (RQ).	19

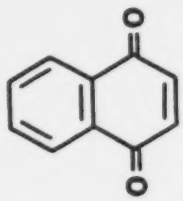
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
BODT	Biological oxygen demand, theoretical
CAS	Chemical Abstract Service
GSH	Reduced glutathione
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
MED	Minimum effective dose
ppm	Parts per million
RQ	Reportable quantity
UV	Ultraviolet

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

1,4-Naphthoquinone is also known as 1,4-naphthalene dione, alpha-naphthoquinone and 1,4-dihydro-1,4-diketonaphthalene. The structure, molecular weight, empirical formula and CAS Registry number are as follows:



Molecular weight: 158.15

Empirical formula: $C_{10}H_6O_2$

CAS Registry number: 130-15-4

1.2. PHYSICAL AND CHEMICAL PROPERTIES

1,4-Naphthoquinone occurs as a greenish-yellow powder or as yellow triclinic needles (U.S. EPA, n.d.). Selected chemical and physical properties are listed below:

Melting point:	123-126°C	Hawley, 1981
Boiling point:	100°C (sublimes)	Hawley, 1981
Water solubility (25°C):	200 mg/ℓ	U.S. EPA, 1985
Vapor pressure:	not available	
Log K_{ow}:	1.78	Hansch and Leo, 1985
Specific gravity (0°C):	1.422	Windholz, 1983
Vapor density (air=1):	5.46	Verschueren, 1983
Conversion factors:	1 mg/m³ = 0.15 ppm 1 ppm = 6.5 mg/m³	Verschueren, 1983

1.3. PRODUCTION DATA

The TSCA Inventory (U.S. EPA, 1977) reported no production sites for 1,4-naphthoquinone in the United States, although the following importers and corresponding import volumes were listed:

	Annual Import Volume (pounds)
Nissho-Iwai American Corp.	1,000,000-10,000,000
Aceto Chemical Co.	10,000-100,000
Nagase American Corp.	10,000-100,000
Sumitomo Shoji America, Inc.	none
GAF Corp.	none

In 1983, 61,260 pounds of 1,4-naphthoquinone were imported into the United States (USITC, 1984). Oxidation of the corresponding amino naphthol produces a high yield of 1,4-naphthoquinone (Thirtle, 1968).

1.4. USE DATA

1,4-Naphthoquinone is used as a polymerization regulator for rubber and polyester resins and in the synthesis of dyes and pharmaceuticals (Hawley, 1981). In addition, it is also used as a fungicide and algicide (Hawley, 1981).

1.5. SUMMARY

1,4-Naphthoquinone is a solid at room temperature. No sites for production of this compound were reported in the United States; however, five importers were listed in the TSCA Inventory (U.S. EPA, 1977). In 1983, a total of 61,260 pounds of 1,4-naphthoquinone were imported (USITC, 1984). 1,4-Naphthoquinone is used as a polymerization regulator for rubber and polyester resins, in the synthesis of dyes and pharmaceuticals, and as a fungicide and algicide (Hawley, 1981).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

U.S. EPA (1985) stated that potential for degradation or elimination of 1,4-naphthoquinone from a river reach traversed in 5 days is very low (~0.00%).

2.1.1. Hydrolysis. Pertinent data regarding the hydrolysis of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

2.1.2. Oxidation. Pertinent data regarding the oxidation of 1,4-naphthoquinone were not located. Like other quinones, 1,4-naphthoquinone can interconvert with its corresponding hydroquinone in an oxidation reduction system (U.S. EPA, n.d.).

2.1.3. Photolysis. Hashimoto et al. (1975) reported that 1,4-naphthoquinone can undergo photoreduction in water by formation of anion radicals by electron transfer from HO radicals and by nucleophilic addition of HO radicals. Potential for photolysis is also suggested by absorption of UV light in the environmentally significant range, wavelengths >290 nm (Finley, 1982).

2.1.4. Microbial Degradation. Heukelekian and Rand (1955) measured a 38% BODT after incubating 1,4-naphthoquinone for 5 days in standard dilution water using sewage as seed; however, this information alone is insufficient for determining the role of microbial degradation in ambient waters.

2.1.5. Volatilization. Pertinent data regarding the volatilization of 1,4-naphthoquinone from water were not located; however, U.S. EPA (1985) stated that it is not expected to evaporate from water.

2.1.6. **Bioaccumulation.** Experimental bioconcentration data for 1,4-naphthoquinone were not located; however, BCFs were estimated from the log K_{ow} of 1.78 and water solubility of 200 mg/ℓ using the following equations (Lyman et al., 1982):

$$\log BCF = 0.76 \log K_{ow} - 0.23 \quad (2\text{-}1)$$

$$\log BCF = 2.791\text{-}0.564 \log S \quad (2\text{-}2)$$

BCF values of 13 and 31 were calculated from Equations 2-1 and 2-2, respectively. These values suggest that there is a slight potential for bioaccumulation to occur in aquatic organisms.

2.1.7. **Adsorption.** Pertinent data were not located regarding the adsorption of 1,4-naphthoquinone to suspended solids and sediments; however, bottom sediment accumulation has been estimated to be 13.8 times greater than ambient water concentration (U.S. EPA, 1985).

2.2. AIR

Pertinent data regarding the fate and transport mechanisms of 1,4-naphthoquinone in the atmosphere could not located in the available literature as cited in the Appendix. Potential for direct photolysis is indicated by a UV absorption maximum (in acetonitrile) at wavelengths of 330 nm (Finley, 1982).

2.3. SOIL

2.3.1. **Chemical Degradation.** Pertinent data regarding the chemical degradation of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

2.3.2. **Microbial Degradation.** Sims and Overcash (1983) reported that 1,4-naphthoquinone at an initial concentration of 500 µg/g soil had a biodegradation half-life of 1.2 minutes. Decomposition of this compound by the soil microbe, Cunninghamella elegans, and a variety of other soil fungi

in culture has been studied (Cerniglia and Gibson, 1977; Cerniglia et al., 1978), although the applicability of these studies to environmental conditions is not known.

2.3.3. **Volatilization.** Pertinent data regarding the volatilization of 1,4-naphthoquinone from soil surfaces were not located. The extent of volatilization is inversely related to the extent of chemical transformation, microbial degradation and adsorption to soils.

2.3.4. **Adsorption.** Since pertinent data were not located regarding the adsorption of 1,4-naphthoquinone to soils, K_{oc} values were estimated from physical properties (Table 2-1). These estimated K_{oc} values indicate that the compound is slightly to moderately mobile in soils (Swann et al., 1983).

2.4. SUMMARY

In water, 1,4-naphthoquinone can undergo photoreduction by reaction with HO radicals (Hashimoto et al., 1975). Potential for photolysis is also suggested by absorption of light wavelengths in the environmentally significant range (Finley, 1982). U.S. EPA (1985) reported that elimination or degradation and volatilization of 1,4-naphthoquinone from water is not expected. BCFs estimated from physical properties suggest that there is a slight potential for bioaccumulation to occur in aquatic organisms. The estimated concentration in bottom sediment is 13.8 times greater than its concentration in ambient water (U.S. EPA, 1985).

In air, potential for photoysis is indicated by a UV absorption maximum (in acetonitrile) at a wavelength of 330 nm (Finley, 1982).

Sims and Overcash (1983) reported a significantly short biodegradation half-life for 1,4-naphthoquinone in soil; however, information was insufficient for adequate evaluation of this transformation mechanism. The compound has been predicted to be slightly to moderately mobile in soils, based on estimated K_{oc} values.

TABLE 2-1

Estimated K_{OC} Values for 1,4-Naphthoquinone

Method	K_{OC}	Reference
Log K_{OC} = -0.55 log S (mg/ℓ) + 3.64	237	Lyman et al., 1982
Log K_{OC} = -0.54 log S (mol fraction) + 0.44	885	Lyman et al., 1982
Molecular topology structural analysis	4310	Sabljic, 1984

3. EXPOSURE

Pertinent data regarding the presence of 1,4-naphthoquinone in the environment could not be located in the available literature as cited in the Appendix.

In addition to its potential entry into the environment during transport, processing and use, 1,4-naphthoquinone may also enter the environment as a degradation product of certain naphthalene derivatives (U.S. EPA, n.d.). For example, the pesticide carbaryl is hydrolyzed to 1-naphthol, which then undergoes biooxidation to 1,4-naphthoquinone (Paris et al., 1975; Rajagopal et al., 1984). 1,4-Naphthoquinone might also enter the environment from facilities manufacturing or processing phthalic anhydride by air oxidation of naphthalene, since 1,4-naphthoquinone is an impurity in commercial grade phthalic anhydride manufactured by this method (0.0002 wt. % max.) (Bemis et al., 1982). 1,4-Naphthoquinone particles have been recovered from particulate catches of experimental fluidized-bed coal combustors, another potential source of atmospheric emission (Hunt et al., 1982).

4. PHARMACOKINETICS

Pertinent data regarding the absorption, distribution or excretion of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

In vitro studies with rat liver microsomes and hepatocytes suggest that 1,4-naphthoquinone may be metabolized by one electron reduction to the naphthosemiquinone radical, which may covalently bind with cellular molecules or enter a redox cycle with molecular oxygen, thereby generating active oxygen species (Doherty and Cohen, 1984; Doherty et al., 1984; Thornalley et al., 1984).

5. EFFECTS

5.1. CARCINOGENICITY

1,4-Naphthoquinone is not scheduled for testing by the National Toxicology Program (NTP, 1986). Hartwell (1963) summarized the results of dermal application studies by Takizawa (1940a,b); however, the summary was incomplete and ambiguous.

1,4-Napthoquinone at concentrations of 0.25 and 0.1% in benzene was applied to the skin of mice every 1 or 2 days for what appears to be 200 days (Takizawa, 1940a). Thirty-seven and 39 mice were alive in the 0.25 and 0.1% groups at 200 days, and the duration of the experiment was >200 days. Tumors in the 0.25% group included six skin papillomas, one skin carcinoma and no lung metastases (one papilloma and two lung tumors in 46 benzene controls), and tumors in the 0.1% group included five skin papillomas, three skin carcinomas and three lung metastases. These numbers apparently indicate the number of mice with tumors, but it is unclear if the number examined is the same as the number alive at 200 days. The Hartwell (1963) summary of the Takizawa (1940b) data indicates that dermal application of 0.25 or 0.1% 1,4-naphthoquinone in benzene every 1 or 2 days for what appears to be 200 days produced skin papillomas, skin carcinomas and lung metastases in 11, 3 and 2 mice, respectively. At 200 days, 77 mice were alive and the study duration was at least 557 days, but it is unclear if the number examined is the same as the number alive at 200 days. There were, however, only three animals with papillomas before 200 days. It appears probable that the Takizawa (1940a) and (1940b) data are from the same study. The uncertainty regarding tumor incidences and control information, however, preclude interpretation of these tumor data. NIOSH (1985), however, reported that the Takizawa (1940b) data indicate that 1,4-naphthoquinone is an equivocal tumorigen.

5.2. MUTAGENICITY

1,4-Naphthoquinone was not mutagenic to Salmonella typhimurium strains TA97, TA98 or TA100 when tested at concentrations up to 250 µg/plate in plate incorporation assays with or without S-9 metabolic activation preparation (Sakai et al., 1985).

1,4-Naphthoquinone also was not mutagenic to S. typhimurium TA98 or TA100 when tested with or without S-9 (Onodera et al., 1982).

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

1,4-Naphthoquinone did not interrupt pregnancy in albino mice when administered by gavage at doses up to 600 µg/day on days 6-12 of gestation (Wiesner et al., 1958). Additional information regarding the design or results of the experiment were not reported.

Daily subcutaneous injection of 10 mg 1,4-naphthoquinone for 14 days had no effect (inhibitory activity) on the estrous cycle of four rats of unspecified strain (Rosen and Millman, 1955). The ovarian stimulating effect of pregnant mare serum gonadotrophin in immature female rats was inhibited by in vitro mixture with 1,4-naphthoquinone before subcutaneous injection, however, indicating a gonadotrophic effect.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Although no chronic or subchronic studies of 1,4-naphthoquinone administered orally or by inhalation were found, limited information regarding the subchronic toxicity of 1,4-naphthoquinone administered subcutaneously was reported by Slyusar et al. (1962). Biweekly subcutaneous injections of 0.025 mg/kg in albino rats for 2.5-5 months produced increased spleen, liver

and adrenal weights, dystrophic histological changes in the liver and myocardium, decreased serum albumin and cholinesterase activities, 39% methemoglobinemia, anemia, erthrocytopenia, decreased plasma-SH groups and decreased vitamin C content in unspecified organs. The same effects occurred after daily subcutaneous injections of 0.025 or 0.05 mg/kg for 5-10 days (Slyusar et al., 1962). Subsequently, Slyusar et al. (1964) described more specifically the hematological effects (methemoglobinemia, Heinz bodies, hemolytic anemia) in rats treated intraperitoneally with 0.03 g/kg for 5 days. The two abstracts, however, reported a 1000-fold difference in the administered dose.

5.6. OTHER RELEVANT INFORMATION

An approximate lethal dose of 470 mg/kg was determined for deer mice given single doses of aqueous 1,4-naphthoquinone by gavage and observed for 3 days (Schafer and Bowles, 1985). An intraperitoneal single dose LD_{50} of 5.5 mg/kg was determined for 1,4-naphthoquinone with Swiss mice that were observed for 5 days (Hodnett et al., 1983). Ansbacher et al. (1942) reported a single dose oral LD_{50} of 140 mg/kg for white mice given "oily" solutions of 1,4-naphthoquinone by gavage.

1,4-Naphthoquinone inhibited ascitic sarcoma 180 in Swiss mice (Hodnett et al., 1983) and has been reported to produce membrane damage, increased methemoglobin concentration, decreased GSH concentration and Heinz bodies in human erythrocytes *in vitro* (Miller and Smith, 1970, 1971).

5.7. SUMMARY

Takizawa (1940a,b) suggested that dermal application of 0.25 or 0.1% 1,4-naphthoquinone in benzene to mice every 1 or 2 days for what appears to be 200 days produced low incidences of local papillomas and carcinomas. The significance of these results cannot be ascertained, however, because tumor

incidences were not specifically reported and control data were incomplete in the available summary (Hartwell, 1963) of these studies.

1,4-Naphthoquinone was not mutagenic to S. typhimurium strains TA97, TA98 and TA100 when tested in plate incorporation assays with or without S-9 metabolic activation preparation (Sakai et al., 1985; Onodera et al., 1982).

Information regarding the teratogenicity of 1,4-naphthoquinone was not located. 1,4-Naphthoquinone did not interrupt pregnancy when administered to mice by gavage at doses up to 600 µg/day on days 6-12 of gestation (Wiesner et al., 1958) or affect the estrous cycle of rats when subcutaneously injected at doses of 10 mg/day for 14 days (Rosen and Millman, 1955).

Slyusar et al. (1962) reported that 0.025 mg/kg injected subcutaneously biweekly for 2.5-5 months or daily for 5-10 days produced increased spleen, liver and adrenal weights, dystrophic histological changes in the liver and myocardium, decreased serum albumin and cholinesterase activities, methemoglobinemia, anemia, erythrocytopenia, decreased plasma -SH groups and decreased vitamin C content in unspecified organs. A subsequent report by Slyusar et al. (1964) reported that doses that were 1000-fold higher resulted in similar effects. Additional information regarding the subchronic or chronic toxicity of 1,4-naphthoquinone was not located, although consistent hemolytic effects have been reported in in vitro studies with human erythrocytes (Miller and Smith, 1970, 1971). Single dose oral LD_{50}s in the range of 100-500 mg/kg have been reported for mice (Ansbacher et al., 1942; Schafer and Bowles, 1985).

6. AQUATIC TOXICITY

6.1. ACUTE

Little information is available concerning the acute toxicity of 1,4-naphthoquinone to fish and other aquatic organisms. Fitzgerald et al. (1952) reported that concentrations of 0.3-0.6 mg/ℓ were "toxic," presumably causing some mortality, in 24-48 hours to black crappie, Pomoxis nigromaculatus, emerald shiners, Notropis atherinoides, bluntnose minnows, Pimephales notatus, rock bass, Ambloplites rupestris, and largemouth bass, Micropterus salmoides. No details were provided. Applegate et al. (1957) reported that an unspecified naphthoquinone ("x,x-naphthoquinone") was lethal to rainbow trout, Salmo gairdneri, bluegills, Lepomis macrochirus, and sea lampreys, Petromyzon marinus, in <24 hours at concentrations of 1 or 5 mg/ℓ. These species were unaffected by exposure to 0.1 mg/ℓ for 24 hours. The minimum inhibitory concentration causing 100% inhibition of growth of the protozoan, Trypanosoma cruzi, after 10 days culture was 0.3 mg/ℓ (Boveris et al., 1978). Asashima (1972) reported that sea urchin, Anthocidaris crasspina and Pseudocentrotus depressus, larvae were unaffected by 36-hour exposures to concentrations of $\leq 3 \times 10^{-6}$ M (0.47 mg/ℓ); however, concentrations of $\geq 5 \times 10^{-6}$ M (0.79 mg/ℓ) resulted in the development of pigment-deficient embryos.

6.2. CHRONIC

Pertinent data regarding the chronic toxicity of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

6.3. PLANTS

Information concerning effects of 1,4-naphthoquinone on aquatic plants is summarized in Table 6-1. The most sensitive species tested was the green alga, Dunaliella bioculata, with a 50- to 72-hour LC_{50} of 0.011 mg/ℓ (Heldal et al., 1984).

TABLE 6-1

Toxicity of 1,4-Naphthoquinone to Aquatic Plants

Species	Concentration	Response	Reference
Blue-green algae			
Microcystis aeruginosa	1% saturation	100% mortality	Fitzgerald et al., 1952
General	0.3-0.6 mg/ℓ	100% mortality	
Green algae			
Selenastrum capricornutum	100% saturation	^{14}C fixation was 2% of control values	Giddings, 1979
	10% saturation	^{14}C fixation was 3% of control values	
	1% saturation	^{14}C fixation was 9-14% of control values	
	0.1% saturation	^{14}C fixation was 59% of control values	
	0.01% saturation	^{14}C fixation was 83% of control values	
Dunaliella salina	0.095 mg/ℓ	Total inhibition of motility, 15 minutes	Stom and Roth, 1981
Dunaliella bioculata	0.011 mg/ℓ	50- to 72-hour LC_{50}	Heldal et al., 1984
Chlorella pyrenoidosa	≥1.6 mg/ℓ	Decreased photosynthesis, cell numbers and chlorophyll concentration	Zweig et al., 1968
Nitella sp.	31 mg/ℓ	Inhibition of cytoplasmic streaming, 15 minutes	Stom and Roth, 1981

6.4. RESIDUES

Pertinent data regarding 1,4-naphthoquinone residues in aquatic biota could not be located in the available literature as cited in the Appendix.

6.5. OTHER RELEVANT INFORMATION

Dierickx (1984) obtained edenzyme extracts from isopod crustaceans, Asellus aquaticus, insects, Notonecta glauca, and snails, Lymnaea peregra, and reported that 1,4-naphthoquinone inhibited glutathione-S-transferase activity in all three aquatic macroinvertebrates in vitro.

6.6. SUMMARY

Little information is available concerning the toxicity of 1,4-naphthoquinone to aquatic organisms. Concentrations of 0.3-0.6 mg/ℓ were reported to be toxic to several fish species (Fitzgerald et al., 1952). The most sensitive aquatic species tested was the green alga, Dunaliella bioculata, with a 50- to 72-hour LC_{50} of 0.011 mg/ℓ (Heldal et al., 1984).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Pertinent U.S. guidelines and standards, including EPA ambient water and air quality criteria, drinking water standards, FAO/WHO ADIs, EPA or FDA tolerances for raw agricultural commodities or foods, and ACGIH, NIOSH or OSHA occupational exposure limits could not be located in the available literature as cited in the Appendix. The recommended drinking water limit in the Netherlands is 0.1 ppm (U.S. EPA, 1985).

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of 1,4-naphthoquinone could not be located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

Takizawa (1940a,b) suggested that dermal application of 0.25 or 0.1% 1,4-naphthoquinone in benzene to mice every 1 or 2 days for what appears to be 200 days produced low incidences of local papillomas and carcinomas. An assessment of carcinogenic potential cannot be determined, however, because tumor incidences were not specifically reported and control data were incomplete in the available summary (Hartwell, 1963) of these studies. 1,4-Naphthoquinone was not mutagenic to S. typhimurium strains TA97, TA98 and TA100 when tested in plate incorporation assays with or without S-9 metabolic activation preparation (Sakai et al., 1985; Onodera et al., 1982).

Data regarding the teratogenicity of 1,4-naphthoquinone could not be located in the available literature. 1,4-Naphthoquinone did not interrupt pregnancy when administered to mice by gavage at doses up to 600 µg/day on days 6-12 of gestation (Wiesner et al., 1958) or affect the estrous cycle of rats when subcutaneously injected at doses of 10 mg/day for 14 days (Rosen and Millman, 1955).

Slyusar et al. (1962) reported that 0.025 mg/kg injected subcutaneously biweekly for 2.5-5 months or daily for 5-10 days produced increased spleen, liver and adrenal weights, dystrophic histological changes in the liver and myocardium, decreased serum albumin and cholinesterase activities, methemoglobinemia, anemia, erythrocytopenia, decreased plasma-SH groups and decreased vitamin C content in unspecified organs. Calculation of an RfD (formerly ADI) from these data is precluded by the limitations in the available data (ambiguous and incomplete report), the origin of the study and the lack of corroborating subchronic or chronic data. Additionally, there is uncertainty regarding the magnitude of doses in the Slyusar et al. (1962)

study, since an abstract of a subsequent report by Slyusar et al. (1964) reported that 1000-fold higher doses resulted in similar effects. Carcinogenicity data are inadequate; therefore, 1,4-naphthoquinone is classified in IARC Group 3 and CAG Group D (U.S. EPA, 1984), which means that there is no evidence of its carcinogenicity in humans.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

Slyusar et al. (1962) reported that 0.025 mg/kg 1,4-naphthoquinone injected subcutaneously biweekly for 2.5-5 months or daily for 5-10 days produced increased spleen, liver and adrenal weights, dystrophic histological changes in the liver and myocardium, decreased serum albumin and cholinesterase activities, methemoglobinemia, anemia, erythrocytopenia, decreased plasma -SH groups and decreased vitamin C content in unspecified organs. Additional information regarding the subchronic or chronic toxicity of 1,4-naphthoquinone was not located, although consistent hemolytic effects have been reported in in vitro studies with human erythrocytes (Miller and Smith, 1970, 1971).

Information regarding teratogenicity of 1,4-naphthoquinone was not located. 1,4-Naphthoquinone did not interrupt pregnancy when administered to mice by gavage at doses up to 600 µg/day on days 6-12 of gestation (Wiesner et al., 1958) or affect the estrous cycle of rats when subcutaneously injected at doses of 10 mg/day for 14 days (Rosen and Millman, 1955).

Calculation of an RQ from the above reports is precluded by the quality of the subchronic toxicity data and the inappropriate route of administration used (Slyusar et al., 1962), and the lack of effects and inappropriate route in the reproductive studies (Wiesner et al., 1958; Rosen and Millman, 1955). Additionally, there is uncertainty regarding the magnitude of dosage in the Slyusar et al. (1962) report since an abstract of a subsequent report by Slyusar et al. (1964) reported that doses that were 1000-fold higher resulted in similar effects. Therefore, data are insufficient to derive an RQ (Table 9-1).

TABLE 9-1

1,4-Naphthoquinone

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:

Dose:

Effect:

Reference:

RV_d:

RV_e:

Composite Score:

RQ: Data are not sufficient for deriving an RQ.

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Takizawa (1940a,b) suggested that dermal application of 0.25 or 0.1% 1,4-naphthoquinone in benzene to mice every 1 or 2 days for what appears to be 200 days produced low incidences of local papillomas and carcinomas. The significance of these results cannot be ascertained, however, because tumor incidences were not specifically reported and control data were incomplete in the available summary (Hartwell, 1963) of these studies. 1,4-Naphthoquinone is not scheduled for testing by the National Toxicology Program (NTP, 1986); therefore, an F factor cannot be calculated.

1,4-Naphthoquinone was not mutagenic to S. typhimurium strains TA97, TA98 and TA100 when tested in plate incorporation assays with or without S-9 metabolic activation preparation (Sakai et al., 1985; Onodera et al., 1982).

Therefore, the data are inadequate and 1,4-naphthoquinone is appropriately placed in IARC Group 3 and CAG Group D (U.S. EPA, 1984), meaning the compound cannot be directly ranked under the CERCLA Hazard Ranking Scheme for Reportable Quantities.

naphthoquinone

10. REFERENCES

Ansbacher, S., W.C. Corwin and B.G.H. Thomas. 1942. Toxicity of menadione, menadiol and esters. J. Pharmacol. Exp. Therapeutics. 75: 111-124.

Applegate, V.C., J.H. Howell, A.E. Hall, Jr. and M.A. Smith. 1957. Toxicity of 4346 chemicals to larval lampreys and fishes. Special Scientific Reports - Fisheries No. 207. Fish and Wildlife Service, U.S. Dept. of Interior, Washington, DC.

Asashima, M. 1972. Formation of pigment-deficient luteus larvae of sea urchins by treatment with α-naphthoquinone. J. Fac. Sci., Univ. Tokyo, Sect. 4. 12: 457-463.

Bemis, A.G., J.A. Dindorf, B. Horwood and C. Samans. 1982. Phthalic acids. In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 17, 3rd ed., M. Grayson and D. Eckroth, Ed. John Wiley and Sons, Inc., New York. p. 741-743.

Boveris, A., A.O.M. Stoppani, R. Docampo and F.S. Cruz. 1978. Superoxide anion production and trypanocidal action of naphthaquinones on Trypanosoma cruzi. Comp. Biochem. Physiol. C. 61C(2): 327-329.

Cerniglia, C.E. and D.T. Gibson. 1977. Metabolism of naphthalene by Cunninghamella elegans. Appl. Environ. Microbiol. 34(4): 363-370.

Cerniglia, C.E., R.L. Hebert, P.J. Szaniszlo and D.T. Gibson. 1978. Fungal transformation of naphthalene. Arch. Microbiol. 117(2): 135-143.

Dierickx, P.J. 1984. Glutathione S-transferase in aquatic macroinvertebrates and its interaction with different organic micropollutants. Sci. Total Environ. 40: 93-102.

Doherty, M.D. and G.M. Cohen. 1984. Metabolic activation of 1-naphthol by rat liver microsomes to 1,4-naphthoquinone and covalent binding species. Biochem. Pharmacol. 33: 3201-3208.

Doherty, M.D., G.M. Cohen and M.T. Smith. 1984. Mechansims of toxic injury to isolated hepatocytes by 1-naphthol. Biochem. Pharmacol. 33(4): 543-549.

Finley, K.T. 1982. In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 19. John Wiley and Sons, Inc., New York. p. 572-577.

Fitzgerald, G.P., G.C. Gerloff and F. Skoog. 1952. Stream pollution: Studies on chemicals with selective toxicity to blue-green algae. Sewage Ind. Wastes. 24(7): 888-896.

Giddings, J.M. 1979. Acute toxicity to Selenastrum carricornutum of aromatic compounds from coal conversion. Bull. Environ. Contam. Toxicol. 23(3): 360-364.

Hansch, C. and A.J. Leo. 1985. Medchem. Project. Pomona College, Claremont, CA.

Hartwell, J.L. 1963. Survey of Compounds which have been Tested for Carcinogenic Activity, 2nd ed. Public Health Service Publ. No. 149, p. 100.

Hashimoto, S., H. Takashima and M. Onohara. 1975. Photochemical reaction of p-benzoquinone and 1,4-naphthoquinone in water. Nippon Kagaku Kaishi. 6: 1019-1023. (CA 83:113339z)

Hawley, G.G. 1981. The Condensed Chemical Dictionary, 10th ed. Van Nostrand Reinhold Co., New York. p. 715.

Heldal, M., S. Norland, T. Lien, G. Knutsen, K. Tjessem and A. Aarberg. 1984. Toxic responses of the green alga Dunaliella bioculata (Chlorophycea, Volvocales) to selected oxidized hydrocarbons. Environ. Pollut. Serv. A. 34(2): 119-132.

Heukelekian, H. and M.C. Rand. 1955. Biochemical oxygen demand of pure organic compounds. J. Water Pollut. Control. Assoc. 27(9): 1040-1053.

Hodnett, E.M., C. Wongwiechintana, W.J. Dunn, II and P. Marrs. 1983. Substituted 1,4-naphthoquinones vs. the ascitic sarcoma 180 of mice. J. Med. Chem. 26: 570-574.

Hunt, G.T., R.J. Kindya, R.R. Hall, P.F. Fennelly and M. Hoyt. 1982. The polycyclic aromatic environment of the fluidized-bed coal combustion process -- An investigation of chemical and biological activity. Polynucl. Aromat. Hydrocarbons: Phys. Biol. Chem. Int. Symp., 6th. Meeting Date, 1981. p. 367-381.

Lyman, W.J., W.F. Reehl and D.H. Rosenblatt. 1982. Handbook of Chemical Property Estimation Methods. McGraw-Hill Book Co., New York. p. 4-9, 5-6.

Miller, A. and H.C. Smith. 1970. Intracellular and membrane effects of oxidant agents on normal red cells. Br. J. Haematol. 19: 417-428.

Miller, A. and H.C. Smith. 1971. Influence of glucose and exogenous glutathione on the red cell membrane effect of the antimalarial drugs 1,4-naphthoquinone and β-naphthol. Br. J. Haematol. 20: 599-609.

NIOSH (National Institute for Occupational Safety and Health). 1985. RTECS (Registry of Toxic Effects of Chemical Substances). Online: October, 1985.

NTP (National Toxicology Program). 1986. Management Status Report. 3/12/86.

Onodera, S., Y. Usui, M. Fuji and S. Suzuki. 1982. Chemical changes of some organic compounds in chlorinated water vs. mutagenicity of ether extractable products obtained by the reaction of naphthols and hypochlorite in dilute aqueous solution. Eisei Kagoku. 28(3): 160-163. (Jap.) (CA 97:210080e)

Paris, D.F., D.L. Lewis, J.T. Barnett, Jr. and G.L. Baughman. 1975. Microbial degradation and accumulation of pesticides in aquatic systems. NTIS PB 241293. 54 p.

Rajagopal, B.S., V.R. Rao, G. Nagendrappa and N. Sethunathan. 1984. Metabolism of carbaryl and carbofuran by soil-enrichment and bacterial cultures. Can. J. Microbiol. 30(12): 1457-1465.

Rosen, F. and N. Millman. 1955. Anti-gonadotrophic activities of quinones and related compounds. Endocrinology. 57: 466-471.

Sabljic, A. 1984. Predictions of the nature and strength of soil sorption of organic pollutants by molecular topology. J. Agric. Food Chem. 32: 243-246.

Sakai, M., D. Yoshida and S. Mizusaki. 1985. Mutagenicity of polycyclic aromatic hydrocarbons and quinones in Salmonella typhimurium TA97. Mutat. Res. 156(1-2): 61-67.

Schafer, E.W., Jr. and W.A. Bowles, Jr. 1985. Acute oral toxicity and repellency of 933 chemicals to house and deer mice. Arch. Environ. Contam. Toxicol. 14(1): 111-129.

Sims, R.C. and M.R. Overcash. 1983. Fate of polynuclear aromatic compounds (PNAs) in soil-plant systems. Residue. Rev. 88: 1-68.

Slyusar, M.P., N.M. Vasilenko and L.T. Kirichek. 1962. Toxicity of some quinones. Nauchn. Tr. Ukr. Nauchn.-Issled. Inst. Gigieny Truda i Prof-zabolevanii. 29: 75-82. (CA 60:16408b)

Slyusar, M.P., N.M. Vasilenko and V.V. Labunskii. 1964. Data on the toxicology of α-naphthoquinones and its permissible concentration in a working area. Gigiena sb., 95-100. (CA 63:13924e)

Stom, D.I. and R. Roth. 1981. Some effects of polyphenols on aquatic plants: I. Toxicity of phenols in aquatic plants. Bull. Environ. Contam. Toxicol. 27(3): 332-337.

Swann, R.L., D.A. Laskowski, P.J. McCall, K. Vander Kuy and H.J. Dishburger. 1983. A rapid method for the estimation of the environmental parameters octanol/water partition coefficient, soil sorption constant, water to air ratio, and water solubility. Residue. Rev. 85: 17-28.

Takizawa. 1940a. No title provided. Gann. 34: 158-160. (Cited in Hartwell, 1963)

Takizawa. 1940b. No title provided. Proc. Imp. Acad., Japan. 16: 309-312. (Cited in Hartwell, 1963)

Thirtle, J.R. 1968. Quinones. In: Kirk-Othmer Encyclopedia of Chemical Technology, 2nd ed., Vol. 16, A. Standen, Ed. John Wiley and Sons, Inc., New York.

Thornalley, P.J., M.D. Doherty, M.T. Smith, J.V. Bannister and G.M. Cohen. 1984. The formation of active oxygen species following activation of 1-naphthol, 1,2- and 1,4-naphthoquinone by rat liver microsomes. Chem.-Biol. Interact. 48(2): 195-206.

U.S. EPA. n.d. OTS Summary. 1,4-Naphthoquinone. Office of Toxic Substances, U.S. EPA, Washington, DC.

U.S. EPA. 1977. Computer print-out of non-confidential production data from TSCA inventory OPTS, CID, U.S. EPA, Washington, DC.

U.S. EPA. 1984. Proposed Guidelines for Carcinogen Risk Assessment. Federal Register. 49(227): 46294-46301.

U.S. EPA. 1985. OHM-TADS (Oil and Hazardous Materials Technical Assistance and Data System). Online: October, 1985.

USITC (U.S. International Trade Commission). 1984. Imports of benzenoid chemicals and products, 1983. USITC, Washington, DC. p. 23.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., New York. p. 900-901.

Wiesner, B.P., M. Wolfe and J. Yudkin. 1958. Effects of some antimitotic compounds on pregnancy in the mouse. Proc. Soc. Study Fertil. 9: 129-136.

Windholz, M. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ. p. 6247-6248.

Zweig, G., J.E. Hitt and R. McMahon. 1968. Effect of certain quinones, diquat, and diuron on Chlorella pyrenoidosa emerson strain. Weed Sci. 16: 69-73.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CASR online (U.S. EPA Chemical Activities Status Report)
CAS online STN International
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in October, 1985. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1985. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH.

ACGIH (American Conference of Governmental Industrial Hygienists). 1985. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1985-1986. Cincinnati, OH. 114 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., Littleton, MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

NTP (National Toxicology Program). 1986. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, N.I. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1984. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1985. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1985. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422, Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.